Non-Technical Abstract

Human Immunodeficiency virus (HIV) infects human white blood cells, including $CD4^+$, co-receptor positive T-cells in the blood. Other cells in the body can also be affected by the virus, such as nerve cells that can result in brain damage. The infected patient will lose many of its $CD4^+$ T-cells and will over time be more and more susceptible to other infections as well as other diseases like cancer. Although recent advances in HIV treatment have slowed the progression of HIV disease for many infected patients on treatment and contributed to the decline in AIDS incidence, many HIV-infected individuals do not respond and/or cannot tolerate these combination drug therapies.

This study will test a new form of therapy to find out if it is safe and effective as an additional treatment for patients with advanced HIV-1 Infection for whom combination drug therapies are failing. The therapy is called "Intracellular Antibody Gene Therapy". Antibodies are molecules made by special blood cells in the body that can bind to infectious agents like bacteria and virus and clear them from the body. The antibody that we will use to treat patients has been designed so that it can stay inside the cell after it has been made. The antibody binds and destroys an important part of the AIDS virus, the Tat protein of the virus. Since the antibody is doing this inside the cell the virus has attacked, we hope that the virus will be crippled in the infected cell so that the cell will not follow the instructions of the virus to become a virus factory to produce new viruses that can infect new cells. We hope that the patients $CD4^+$ T-cells that have been treated will be protected from HIV infection when they are put back into the body, and if they become infected with HIV this results in production of less viruses.

In this study we will test if it is safe to introduce a gene for an intracellular antibody in ten HIV-1-infected patients that are sustaining detectable HIV-1 levels in their blood despite combination anti-retroviral therapies. We will isolate blood $CD4^+$ T-cells from the patient and thereafter introduce the antibody gene with help of a retroviral vector. This vector will carry the antibody gene, $sFvhutat_2$, into the cells. After this has been done the cells will be given back to the patient. We are then going to study how well the cells will survive in the patient and if they will result in any negative effects on the body. The results of these studies will determine if this intracellular antibody can protect $CD4^+$ T-cells in patients with advanced HIV infection. The results will also help in the design of future trials of larger scale T cell replacement and of bone marrow stem cell gene therapies for HIV infection.